

### **REMARKS**

The Abstract is shortened.

Claim 1 is amended to remove the word “platform” and correct a typographical error.

Claim 9 is cancelled.

Claim 10 is amended to correct the claim dependency.

No new matter is added in the above amendment. The Examiner is requested to enter the amendment and reconsider the application.

### **OBJECTION TO THE SPECIFICATION**

Examiner objected to the abstract of the disclosure as being over 150 words.

The abstract of the disclosure has been amended to reduce the number of words to under 150 words.

In view of the above comments and foregoing amendments, Examiner is respectfully requested to withdraw the objections to the specification.

### **CLAIM REJECTIONS - 35 USC § 112**

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Examiner states that in claim 1, the recitation, “platform plant” in lines 3 and 7 renders the claim indefinite.

Claim 1 has been amended to remove the term “platform”, to clarify claim 1.

Examiner states that in claim 9 the recitation “pharmaceutical active protein”, renders the claim indefinite as it is unclear what is considered to be a “pharmaceutical active protein”.

Applicants respectfully submit that a person of skill in the art would readily understand the meaning of the term “pharmaceutically active protein” as any protein which has pharmaceutical activity. However, to further the prosecution, Applicants have cancelled Claim 9.

In view of the above comments and foregoing amendments, Examiner is respectfully requested to withdraw the rejection of claims 1-8 and 10 as being indefinite under 35 U.S.C. 112, second paragraph.

### CLAIM REJECTIONS - 35 USC § 103

Claims 1-10 and 14 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Fabijanski et al. (US Patent No. 6,753,460) in view of Mason et al. (1992, *PNAS* 89:11745-11749) and Chou et al. (1998, *PNAS* 95:5293-5298). Applicant respectfully traverses the rejection.

The present invention as defined in both claim 1 and claim 14, and as shown in Figure 2, provides a coding region of interest and its associated regulatory region (second coding region (70) and second regulatory region (60), respectively) on the second nucleotide sequence (50) together with a coding region encoding a repressor (95) and its associated regulatory region (third coding region (90) and third regulatory region (80), respectively). The first nucleotide sequence (10) has a coding region for a tag protein (35; first coding region (30)), which is in operative association with a first regulatory region (20) and an operator sequence (40). In a dual transgenic plant transformed with both the first and second nucleotide sequence, expression of the second nucleotide sequence (50) produces the repressor (95) which is capable of binding to the operator sequence (40) in the first nucleotide sequence (10), thereby inhibiting expression of the tag protein (35). The method of claims 1 and 14 also includes the step of selecting for the dual transgenic plant. As stated at page 23, line 17 to page 24, line 5 of the present application:

“Selecting may involve, but is not limited to, detecting the presence of the tag protein (35), activity associated with the tag protein (35), or expression of the first coding region (30) using standard methods. If the tag protein is a marker such as a GFP, then the presence of GFP may be detected using standard methods, for example using UV light. If the tag protein is an enzyme or an antigen, this activity can be assayed, for example assaying for GUS activity, or an ELISA or other suitable test, respectively. Similarly, the expression of the first nucleic acid sequence may be determine by assaying for the transcript, for example but not limited to, using Northern hybridization, S1 nuclease, array analysis, PCR, or other methods as would be known to one of skill in the art. If the tag protein is a conditionally lethal sequence, then in the presence of a toxic substrate, alteration in the growth, the development, or killing, of the plant or portion thereof, occurs and identifies plants that express the first coding region (30) encoding the tag

protein (35; in this case a conditional lethal protein). In this way selecting may be used to differentiate between a plant which lacks the second nucleotide sequence (50) comprising the coding region of interest (70) and the third gene that encodes the repressor (90), from a plant that expresses the second nucleotide sequence (50), since if the repressor is present, then the repressor binds the operating sequence (40) of the first nucleotide sequence (10), and inhibits or reduces expression of the first coding region (30), and tag protein levels are reduced. Conversely, if the tag protein is present, then visual inspection of the plant or portion thereof indicates either that the first nucleotide construct has been introduced into the plant, as in i) above, or that the plant or portion thereof has not been transformed with the second nucleotide sequence, as in ii) above.”

Fabijanski et al., describes a genetic system comprising two DNA constructs. One DNA construct comprises a dominant repressible lethal gene, that, when active, results in cellular death, and whose expression is inhibited in plant cells which contain a second DNA construct comprising a repressor gene. The repressible lethal gene may be linked to a gene encoding a novel trait.

As stated by Examiner, Fabijanski et al. do not include a second coding region encoding a gene of interest and the second regulatory region in the second nucleotide sequence of step ii). In other words, the gene encoding a novel trait (second coding region encoding a gene of interest) is found on the DNA construct (first nucleotide sequence) comprising the repressible lethal gene (first coding region encoding a tag protein), instead of on the DNA construct (second nucleotide sequence) comprising the repressor gene (third coding region encoding a repressor). There is no hint or suggestion in Fabijanski et al. that the gene encoding a novel trait (second coding region encoding a gene of interest) could be positioned on the DNA construct (second nucleotide sequence) comprising the repressor gene (third coding region encoding a repressor). In fact, Fabijanski et al. teaches away from this embodiment, as it is disclosed “[L]inkage of the novel trait to the repressible lethal gene ensures that the novel trait can not persist in related species by transfer through sexual crossing” (column 7, lines 35-37).

Examiner alleges that it would have been obvious and within the scope for a person with ordinary skill in the art to modify the method taught of Fabijanski et al. by adding the

expression cassette of Mason et al. into the vector expressing tet repressor gene. Applicants respectfully disagree.

Mason et al. teach transgenic tobacco plants expressing the hepatitis B surface antigen under the control of CaMV 35S promoter. There is no hint or suggestion in Mason et al. that the expression cassette comprising a gene encoding hepatitis B surface antigen linked to a CaMV 35S promoter would be added into a vector expressing a tet repressor gene. Examiner alleges “[O]ne would have been motivated to do so given the teaching of Mason et al. that hepatitis B surface antigen could be used as a vaccine against hepatitis B virus infection as well as the teaching of Fabijanski et al. that the genes of repressor and repressible lethal gene are linked and may further comprise a novel trait”. Applicants respectfully disagree.

Even if a skilled person were motivated by the teaching of Mason et al. to modify the method taught of Fabijanski et al. (which is denied), the expression cassette comprising a gene encoding hepatitis B surface antigen linked to a CaMV 35S promoter would be inserted in the DNA construct comprising the repressible lethal gene as a gene encoding a novel trait, and not on the construct comprising the tet repressor gene. As mentioned above, Fabijanski et al. actually teaches away from addition of the expression cassette of Mason et al. into the vector expressing tet repressor gene, as it is disclosed “[L]inkage of the novel trait to the repressible lethal gene ensures that the novel trait can not persist in related species by transfer through sexual crossing” (column 7, lines 35-37).

In order to set forth a *prima facie* case of obviousness under 35 U.S.C. 103(a), the combination of the cited references must actually teach or suggest the claimed invention. Applicant respectfully submits that even if a combination of Mason et al. and Fabijanski et al. could be made (which is denied), it is submitted that the skilled person would still not arrive at the claimed invention.

Applicants respectfully request that Examiner point to the passage in Fabijanski et al. which teaches that the genes of repressor and repressible lethal gene are linked and may further comprise a novel trait, in order that they may further comment on Examiner’s comments regarding the motivation for combining Mason et al. and Fabijanski et al. to arrive at the present invention.

As stated by Examiner, Chou et al. teach the zinc finger gene from *Agrobacterium*, Ros, and repression of the *virC/D* and *ipt* genes by binding of Ros to the conserved operator “ros box”. There is no teaching in Chou et al. that would motivate or lead a person of

ordinary skill to provide the coding region of interest and its associated regulatory region (second coding region (70) and second regulatory region (60) respectively) on the second nucleotide sequence (50) together with a coding region encoding a repressor (95) and its associated regulatory region (third coding region (90) and third regulatory region (80) respectively), as is required by the present invention.

Only the present invention teaches a method of selecting for a plant or portion thereof that comprises a coding region of interests, where the coding region of interest and its associated regulatory region are on the second nucleotide sequence together with a coding region encoding a repressor and its associated regulatory region. Neither Mason et al., Fabijanski et al. nor Chou et al. hint or suggest such a method. "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" *W.L. Gore & Associates, Inc. v. Garlock Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983). Applicant respectfully submits that the Examiner has only arrived at the present invention from the combination of Fabijanski et al., Mason et al. and Chou et al. through the benefit of impermissible hindsight.

Examiner also alleges that it would also have been obvious for a person with ordinary skill in the art to modify the repressible phaseolin promoter of Fabijanski et al. by replacing the tet operator with the Ros operator of Chou et al. and cross the transformed tobacco carrying a repressible lethal gene under the control of a modified phaseolin promoter with tobacco that was transformed with a gene encoding a Ros repressor. Applicant respectfully submits that even if a combination of Fabijanski et al. and Chou et al. could be made (which is denied), it is submitted that the skilled person would still not arrive at the claimed invention.

Examiner further alleges that it would have been obvious for a person with ordinary skill in the art to replace the conditional lethal gene, oncogene 1 of Fabijanski et al. by methoxininine dehydrogenase gene, as also suggested by Fabijanski et al. Applicant respectfully submits that even if it would have been obvious for a person with ordinary skill in the art to replace the conditional lethal gene, oncogene 1 of Fabijanski et al. by methoxininine dehydrogenase gene (which is denied), it is submitted that the skilled person would still not arrive at the claimed invention. Fabijanski et al. do not teach the use of a construct encoding a coding region of interest (second coding region) that is localized on a

separate construct from the construct encoding the conditionally lethal gene (i.e. the tag protein, or first coding region). Even if one of skill were to replace the tag protein (first coding region) with the conditionally lethal gene disclosed by Fabijanski, the combination of elements with each of the first second and third nucleotide sequences as defined in claims 1-10 and 14 of the present invention is very different from those disclosed by Fabijanski.

Neither Fabijanski et al., Mason et al. nor Chou et al., singly or in combination, teaches or suggests a method of selecting for a plant or portion thereof that comprises a coding region of interests, where the coding region of interest and its associated regulatory region are on the second nucleotide sequence together with a coding region encoding a repressor and its associated regulatory region. Claims 2-9 ultimately depend from claim 1 and include the limitations thereof. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness for claims 1-10 and 14. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

#### **PROVISIONAL DOUBLE PATENTING REJECTION**

Claims 1-10 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 18-24 of copending Application No. 10/719,996 in view of Mason et al. (1992, *PNAS* 89:11745-11749).

Applicants wish to postpone the response to this provisional rejection until the claims are otherwise allowable.

Claims 1-10 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 21 and 24 of copending Application No. 10/995,951 in view of Mason et al. (1992, *PNAS* 89:11745-11749).

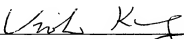
Applicants wish to postpone the response to this provisional rejection until the claims are otherwise allowable.

**CONCLUSION**

In view of the above, examination of the application on the merits and allowance is respectfully requested.

Respectfully submitted,

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